the genesis of pruritus ani. Faeces contain bacteria whose metabolic products include endopeptidases, which can produce itching in experimental conditions.[5 6]

Although dysfunction of the anal sphincter itself may not be the cause of pruritus ani, it may be an important contributing factor. Further studies are required of the action of the sphincters in this condition, together with studies of the faecal and perianal skin flora. Nevertheless, the results reported here suggest an important new approach that may help to elucidate this troublesome ailment.

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SHORT REPORTS

Rotaviruses and the respiratory tract

Rotavirus infection is the commonest cause of acute non-bacterial gastroenteritis in infancy and childhood, but the method by which the virus is transmitted is not established. Several studies, however, have noted an upper respiratory prodrome or concurrent respiratory symptoms and signs in infants and young children with rotavirus-induced gastroenteritis,[1-3] suggesting a possible upper respiratory infection, and this has lead to speculation that transmission may be by respiratory droplet. Two reports have shown that gastroenteritis caused by rotaviruses is associated with otitis media[2 3]; one described it in patients with rotavirus-induced gastroenteritis but not in gastroenteritis caused by other agents. We therefore tried to detect rotavirus in the upper respiratory tract during natural rotavirus infection in neonates and young children admitted to St Thomas's Hospital during the months December 1978 to April 1979.

Patients, methods, and results

Stool specimens were obtained and nasopharyngeal secretions (NPS) were collected by suction catheter within seven days (mean of 3·5 and 3·8 days respectively) of onset of gastrointestinal symptoms from 24 neonates and young children (< 3 years) and from 23 age-matched controls who were in the same ward but not suffering from gastroenteritis. The catheter contents were flushed out with 5-10 ml viral transport medium, mechanically shaken for one hour at 37°C, and an aliquot removed for routine viral isolation in tube cultures of human embryo lung fibroblasts, HeLa, and cynomolgus monkey kidney cells. Nasopharyngeal cells were separated by centrifugation, washed three times in phosphate-buffered saline (PBS), fixed in acetone, and stored at −70°C for subsequent detection of rotavirus by immunofluorescence (IF) employing a swine anti-human rotavirus and a rabbit antiswine FITC conjugate. The supernatant was ultracentrifuged at 100 000 *g* for one hour, the pellet resuspended in 0·5 ml PBS, and examined by negative-staining electronmicroscopy (EM) using 3% phosphotungstic acid pH 6·5, solid phase immune EM (SPIEM), and enzyme-linked immunosorbent assay (ELISA).[4] SPIEM was by a modification of the method described by Derrick.[5] Carbon-coated collodion grids were floated on a drop of 1:100 dilution of a high titre goat antihuman rotavirus antiserum (provided by Dr R H Yolken, NIH, Bethesda) in 0·1 M phosphate buffer pH 7·0 containing 0·1% bacitracin in a humified chamber for 15 minutes. Grids were then washed with 25 drops of buffer, drained, and floated on a drop of the test sample for 15 minutes. After a second buffer washing the grids were washed with five drops of 3% phosphotungstate pH 6·5, drained, dried, and examined in a Philips EM 201C at 100 kv.

Thirteen of the 24 patients with gastroenteritis excreted rotavirus in their stools, 10 having upper respiratory features including coryza, cough, and otitis media. But, despite obtaining NPS from two patients before the onset of their gastrointestinal symptoms, no patients had rotavirus detectable in NPS by EM, SPIEM, or ELISA. Nasopharyngeal cells from all patients were negative for rotavirus by IF. No viruses were isolated from NPS in cell cultures or seen on direct EM. Rotavirus was not detected in NPS or stools from asymptomatic control patients.

Comment

Our preliminary investigations suggest that rotaviruses do not replicate in the nasopharynx: we used highly sensitive tests to detect their presence. We calculated that by direct EM $\geqslant 5\times10^4$ rotavirus particles/ml can be detected. SPIEM and ELISA are more sensitive and can detect $\geqslant 1\times10^4$ particles/ml. Failure to detect rotavirus in respiratory secretions was unlikely to be because virus was no longer being excreted via the respiratory tract by the time gastroenteritis developed, since we obtained NPS from two children one and five days respectively before the onset of gastroenteritis. Why so many patients with rotavirus-induced gastroenteritis have upper respiratory tract features remains to be explained.

We thank Sara Palmer and W Stone for cell culture work.

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Bitter lemon purpura

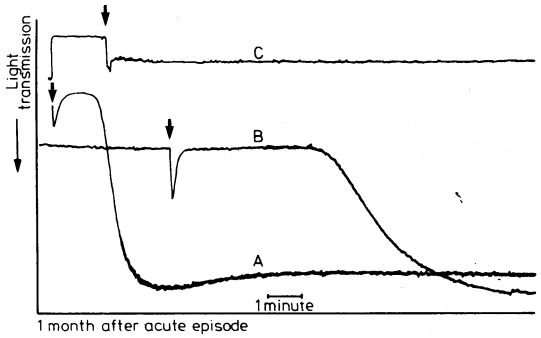
Severe thrombocytopenia due to drug-induced platelet antibodies is relatively unusual, although drugs that can produce this effect are widely encountered. Even the minute amount of quinine present in tonic water (80 μg/ml) is sufficient to cause severe thrombocytopenia ("cocktail purpura").[1] We describe its occurrence in a sensitised individual after drinking a single glass of bitter lemon containing 20 μg/ml/quinine. There was no indication that the brand contained quinine.

Case report

A 16-year-old schoolgirl awoke one morning feeling weak and shivery. Later in the day purpuric haemorrhages appeared on her arms, face, and legs. Six days later she had a severe epistaxis and on admission to hospital was found to have extensive purpura and petechiae. The spleen was impalpable and general physical examination was otherwise normal. Six weeks earlier she had been prescribed quinine sulphate tablets for nocturnal leg cramps, although she admitted to taking tablets irregularly. Investigations showed haemoglobin 11·3 g/dl; white cell count $5\cdot5\times10^9$/l (5500/mm^3); platelet count 15×10^9/l (15 000/mm^3); prothrombin ratio 1·2; partial thromplastin time kinase 39 s; fibrinogen 2·8 g/l. No underlying cause for the thrombocytopenia was found. The marrow aspirate contained normal numbers of megakaryocytes. The diagnosis rested between idiopathic thrombocytopenic purpura and a drug-induced thrombocytopenia. The patient was therefore given a platelet transfusion on admission and started

on 40 mg prednisolone daily. Within 48 hours the platelet count returned to normal. She was allowed home after one week and warned to avoid quinine in any form. Six days later she again developed feverishness and malaise and was admitted with widespread purpura. The platelet count was 18×10^9/l (18 000/mm^3). She was still taking 20 mg prednisolone daily. After admission she rapidly improved and her platelets increased to 50×10^9/l (50 000/mm^3) within 24 hours. She denied taking quinine sulphate tablets, but on the evening before admission she took a glass of sparkling bitter lemon. She had first inspected the label and found no mention of quinine among the ingredients.

That the thrombocytopenia was due to quinine-dependent platelet antibodies was confirmed by standard in-vitro tests of platelet factor 3 release (in which the addition of serum containing the drug-dependent antibody to normal platelet-rich plasma shortens the clotting time by releasing platelet factor 3 from damaged membranes) and platelet aggregometry.[3] The latter provides a simple method for detecting drug-dependent antibodies. In this case aliquots of the patient's platelet-rich plasma (PRP) showed increased light transmission with the addition of a quinine solution (containing 715 μg/ml) and tonic water (80 μg/ml) (figure) but no change with bitter lemon (20 μg/ml). A threshold concentration was obtained with a solution of 35 μg/ml. Below that there was no change in light transmission. Subsequent analysis by light microscopy showed that actual lysis of platelets had occurred, which was found to be complement-dependent (figure). PRP with inactivated complement (heated at 56°C for 10 minutes) showed neither lysis nor aggregation, supporting previous findings that immune lysis can occur in the absence of platelet aggregation.[3]



Increase in light transmission of PRP on addition (↓) of solution containing 715 μg/ml quinine (A). After inactivation of complement same solution produced no response (C). Brisk response with tonic water (B) containing 80 μg/ml quinine.

Comment

Quinine is one of the commonest drugs responsible for drug-induced purpura. It is believed to cause thrombocytopenia by an "innocent bystander" mechanism[4] wherein the drug-antibody complex passively attaches to platelets and results in fixation of complement and subsequent lysis. This case shows that minute amounts can induce severe thrombocytopenia in a previously sensitised person. We were therefore surprised to find that none of the major pharmaceutical organisations has a reference list of quinine-containing substances, which is essential information for people who remain at risk for life. We also think that all products containing quinine should be appropriately labelled.

We thank Dr G J R McHardy for permission to report this case, Dr A C Parker for helpful discussion, and Miss Jo Donnelly for typing the manuscript.

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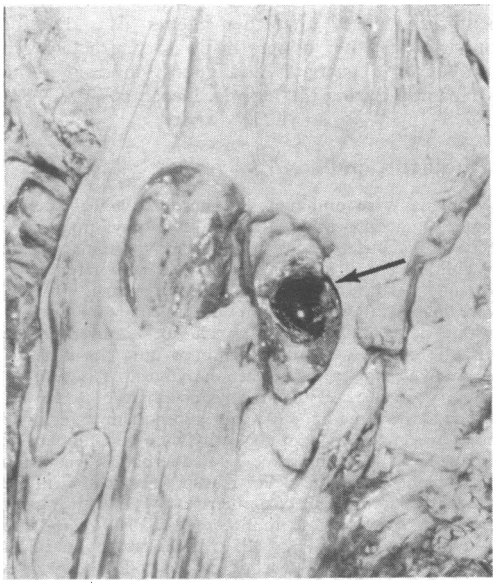
Atrio-oesophageal fistula complicating mitral valve disease

A man with long-standing mitral stenosis and incompetence of rheumatic origin died suddenly with massive haematemesis resulting from a left atrio-oesophageal fistula. We think this is the first report of this dramatic complication of mitral valve disease.

Case report

A 54-year-old Chinese man had a long-standing history of rheumatic heart disease with mitral stenosis and incompetence. In October 1970 he complained of dyspnoea and was started on digoxin, hydrochlorothiazide, and supplementary potassium in the form of a mixture of potassium chloride 1 g thrice daily. He was regularly followed up at the cardiac clinic and maintained on the above medication. In 1977 he was twice admitted to hospital with epigastric pain and melaena. Barium meal radiography showed a peptic ulcer in the posterior wall of the stomach, for which symptomatic treatment with antacids was given. In November 1978 during a routine follow-up visit the potassium chloride mixture was replaced by the more fashionable slow-release potassium chloride tablets (three tablets daily). In July 1979 he was brought to hospital with a massive haematemesis, which was assumed to be the result of an acute exacerbation of the gastric ulcer. He died within 48 hours of admission without recovering from shock. Necropsy confirmed the presence of severe mitral stenosis and incompetence. There was aneurysmal dilatation of the left atrium with marked thinning of the left atrial wall. The oesophagus was displaced posteriorly and compressed. A fistula 1 cm in diameter just below the carina of the trachea connected the posterior wall of the left atrium to the anterior wall of the oesophagus. Over the mucosal surface of the oesophagus, at the site of the fistula, there was an ulcer 2 cm in diameter (figure). Histological examination of the wall of the fistula showed acute inflammation. There was free flow of blood from the left atrium to the oesophagus. The stomach was grossly distended by a huge blood clot.



Oesophagus with mucosal ulcer and opening of fistula (arrowed).

Comment

Small bowel ulceration is a well recognised complication with enteric-coated potassium chloride,[1 2] and there are reports of slow-release potassium chloride tablets causing oesophageal ulceration in circumstances (left atrial dilation in particular) predisposing to oesophageal stasis.[3 4] Pemberton[3] reported oesophageal ulceration in a 44-year-old woman on Slow-K who had recently had a mitral valve replacement, and all the six patients of Whitney and Croxon[4] with oesophageal ulceration had chronic mitral valve disease and had been treated with slow-release potassium chloride. Presumably the oesophageal compression caused by the dilated left atrium results in stasis of the tablet at the site of obstruction, leading to the release of a local high concentration of potassium chloride which is ulcerogenic. Probably the acute inflammation evoked by the ulcer coupled with pressure necrosis led to the development of the fistula in our patient.